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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,793	PARANHOS-BACCALA ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-36,41-43 and 46* is/are pending in the application.

4a) Of the above claim(s) *8-15,17-20,22-36 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,16 and 21* is/are rejected.

7)☒ Claim(s) *7 and 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 5-36, 41-43, and 46 are pending.

Claims 8-15, 17-20, 22-36, and 41-43 are withdrawn.

Claims 1-3, 5-7, 16, 21, and 46 are examined on the merits.

This Office Action is in reply to Applicants' correspondence of 10/23/2006. Applicants' remarks and amendments have been fully considered but are not found to be persuasive. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn. **This Action is made FINAL.**

Claim Objections – New Objection

1. Claim 7 is objected to because of the following informalities:

The claim recites a group of sequences for a nucleic acid molecule where the first member of the group is identified as '(1)', and the second member of the group is identified as '(ii)'. For consistency within the claim, the first member of the group should be identified as '(i)'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 1st Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Although the rejected claims are drawn to products, this rejection is written to address the functional limitations that are recited in the claims and asserted in the specification (i.e. an association with disease). The specification does not provide nucleic acids associated with an autoimmune disease or with an unsuccessful pregnancy or pathological conditions of pregnancy.

Nature of the invention and breadth of the claims

The rejected claims are drawn to nucleic acids encoding an expression product that is immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease (claim 5), and more specifically multiple sclerosis (claim 6).

The claims encompass disease or pathological conditions in any organism.

The claims encompass nucleic acid fragments that are described only by the structure 'a sequence complementary to sequence (i) or (ii)' (as recited in part (iii) of claim 1).

The nature of the invention requires knowledge of an association between a nucleic acid fragment and recognition of the encoded expression product by antibodies present in a biological sample from any patient suffering from any autoimmune disease.

Direction provided by the specification and working example

The specification of the instant application describes the identification of a retroviral-like gene structure, named 'HERV-W' by the applicant, in a placental cDNA

library by testing with Ppol-MSRV (SEQ ID NO: 18) and Penv-C15 (SEQ ID NO: 19) probes and then carrying out gene walking (p.3 lns. 1-10).

The specification of the instant application teaches that applicant envisages the potential role of retroviral type structures in the development of autoimmune disease, in unsuccessful pregnancy or pathological conditions of pregnancy (p.2 lns.18-24).

The specification teaches the sequences of several clones that contain various retroviral-like elements (p.3 lns. 15-35); the specification further teaches that the different clones were subject to sequence alignment to create a putative genetic organization of HERV-W in the RNA form (SEQ ID NO: 30) (pp.4-5).

The specification teaches that homology searching over several databases using 'the reconstructed genome' (presumably SEQ ID NO: 30) identified several related sequences in the human genome. The specification provides a diagrammatic view of the alignment of four clones with the 'reconstructed genome' (Fig 1), and indicates that the reconstructed genome is contained entirely within clone RG083M05 (p.6 ln.13). The specification further teaches that RG083M05 is 96% similar to the reconstructed genome, but indicates that no genomic fragments identified by database searching contained a 'functional gag gene' (p.6 lns.19-20).

The specification further teaches the production of the 'Pgag-C12' probe (SEQ ID NO: 3), which corresponds to the coding region of the clone MSRV gag c12 (Example 1, pp. 10-14). The specification teaches amplification of the MSRV gag gene by RT-PCR from total RNA extracted from plasma from a patient suffering from MS. The specification teaches using the MSRV gag gene probe in a Southern blot analysis

(Monochromosomal Somatic Cell Hybrid blot) to identify gene location and copy number.

In is not clear if applicant intends that amplification of the 'MSRV gag c12' probe creates a nucleic acid sequence equivalent to the 'HERV-W gag gene' of the instant application. In fact, an alignment of the former (SEQ ID NO: 3; p.13 ln.9) with the latter (SEQ ID NO: 2; p. 18 ln 35; the claims are specifically drawn to SEQ ID NO: 2) indicates that the two sequences are not identical.

The specification does not teach the amplification any gag gene by RT-PCR other than the single example of amplification of the MSRV gag gene from the plasma of an MS patient (example 1). The specification does not teach any amplification from any non-MS patient.

The specification describes the amplification of the HERV-W gag gene from isolated human chromosomes (example 2.1), and subsequent analysis of the amplification product by agarose gel and hybridization of the amplification product with the gag c12 probe. The specification does not provide the results of this analysis.

The specification teaches that the PCR products created from the amplification of HERV-W gag genes from individual chromosomes were subjected to in vitro transcription/translation, and the protein products were analyzed by gel electrophoresis. The results indicate that the PCR products of the amplified HERV-W gag gene from chromosomes 1, 3, 6, 7, and 16, upon in vitro transcription/translation, produced proteins of molecular masses ranging from 17-45 kDa (Example 2.2; Table 2).

The specification provides no analysis of the transcription/translation beyond the molecular masses (Table 2) of the protein products. The specification teaches that SEQ ID NO: 2 encodes a protein of approximately 45 kDa (p.22 ln.15); there is no indication as to the source of the mass heterogeneity in the transcription/translation products using the PCR templates. Given the heterogeneity of the products resulting from in vitro transcription/translation, it is notable that there is no analysis of the actual amino acid sequences of any of the protein products; though the specification teaches that the PCR products used as templates for in vitro transcription/translation were sequenced (p.18 lns.21-32) the specification does not provide the results of the nucleic acid sequence analysis.

The specification further teaches the production of a recombinant protein from an expression vector containing the coding region of SEQ ID NO: 2, and reaction of sera with the recombinant protein (Example 3). The results (Table 3) indicate that 6 of 15 'MS', 1 of 2 'Neurological Controls', and 1 of 22 'Healthy Controls' samples showed reactivity to the recombinant protein. The results provide only a qualitative measure of reactivity (i.e.: +++, ++, +, +/-). There is no definition of what is the source of a sample that is a 'Neurological control'. There is no statistical interpretation of the data to examine the significance of the results.

The specification does not provide any analyses related to any diseases other than multiple sclerosis. There is no analysis of biological samples from patients suffering from any other autoimmune disease. There are no analyses pertaining to

biological samples related to unsuccessful pregnancy or any pathological conditions of pregnancy.

There is no analysis of any fragments of SEQ ID NO: 2. Notably, there is no indication of the different expression of any transcription or translation product belonging to SEQ ID NO: 2 but not SEQ ID NO: 1.

The specification provides no analysis of any nucleic acids or transcripts in a disease sample (e.g. autoimmune disease or pathological condition of pregnancy) as compared to any non-disease control sample.

State of the art, level of skill in the art, and level of unpredictability

While the state of the art with regard to identification or production of any nucleic acid of a particular sequence is high, the unpredictability of associating any specific nucleic acid or nucleic acid fragment with a particular pathological condition is even higher.

The prior art does not teach the association of nucleic acid fragments of SEQ ID NO: 2 encoding a portion of a gag gene but not belonging to SEQ ID NO: 1 as being associated with any disease in a statistically significant manner. Given the requirements of claim 1 (and thus the dependent claims 2-7, 16, 37-40), that the nucleic acid fragment encode a portion of the gag gene, and is a fragment of SEQ ID NO: 2 but not SEQ ID NO: 1, and the extremely high degree of identity between SEQ ID NO: 2 and SEQ ID NO: 1 (Blast 2 sequences results: Align Seq ID 1:2), the claims appear to be drawn to a sequence related to positions 374-473 of SEQ ID NO: 2. There is no

indication in either the specification or the prior art that this sequence is associated with any disease or any pathological condition.

While the claims encompass nucleic acid fragments associated with disease and pathologies in any organism, the specification teaches the analysis of nucleic samples only from humans. The prior art of Mayer et al (1998) teaches that related sequences (e.g. the sequence of a gag gene from an endogenous retrovirus) are different among several closely related species, including Humans, green monkeys, and macaque (p.1872 – Sequencing of HERV-K gag genes from lower Old World primates; Fig 6). Thus it is unpredictable as to whether or not the claimed nucleic acid fragments would be applicable to any species other that humans.

The specification teaches the amplification of RNA sequences from samples via RT-PCR. It is, however, not taught that the presence of a nucleic acid in the genome (DNA gene) or expression of the nucleic acid (RNA transcript) is associated with a disease. The post-filing art of Newton et al (2001) teaches the difficulty in applying gene expression results to the association of gene expression with a phenotype. Newton et al teaches that a basic statistical problem is determining when the measured differential expression is likely to reflect a real biological shift in gene expression, and replication of data is critical to validation (p.38, third full paragraph). The specification teaches only the analysis of sera reactivity to recombinant protein. However it is unpredictable as to whether or not such a measure of protein levels is indicative of any nucleic acid expression. The post-filing art of Chan teaches that cells have elaborate regulatory mechanisms at the level of transcription, post-transcription, and post-

translation (p1, last paragraph), and that transcript and protein abundance measurements may not be concordant (p.3, sixth full paragraph). Thus it is unpredictable as to whether or not the claimed nucleic acid fragment or transcription product is associated with any disease or pathological condition.

While the specification asserts that the claimed sequence has potential role in the development of autoimmune disease, in unsuccessful pregnancy or pathological conditions of pregnancy (p.2 lns.18-24), there is a lack of evidence presented to indicate any association of the sequence to such pathologies. The post-filing art reveals that most gene association studies are typically wrong. Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene:disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in gene association studies (middle column, 1st complete paragraph). And while the instant specification provides no statistical analysis regarding the sera reactivity of different samples to a recombinant protein encoded by SEQ ID NO: 2, the prior art of Thisted (1998) provides guidance as to what is required to indicate that an association is statistically significant. Thisted teaches that it has become scientific convention to say that a p-value of 0.05 is considered significant (p.5 - What does it mean to be 'statistically significant'), and that

values above the conventional reference point of 0.05 would not be considered strong enough for the basis of a conclusion.

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to make and use the claimed invention. One would have to perform a large case:control study to examine the large genus of claimed nucleic acid sequences to determine whether or not any claimed sequence is in fact a gag gene of an endogenous retrovirus associated with a disease. This would involve the analysis of many possible different organisms, and also the examination of a large number of diseases. Because of the breadth of the claims as written, one would have to investigate an enormous number of nucleic acid fragments, which minimally need only contain any protein encoding portion of SEQ ID NO: 2, which could be a nucleic acid fragment as few as three nucleotides.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the paucity of working examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention as intended.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 112 1st¶ for lack of enablement. Specifically, the Examiner has rejected claims that recite the functional limitations of the claimed nucleic acids as encoding an expression product 'characterized in that the expression product is immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease', as recited in claim 5.

Initially, Applicants have noted that subject matter from the specification should not be imported into the claims (Remarks p.11, footnote), and have further submitted that functional limitations of a product cannot carry significant weight in an enablement rejection but not in an anticipation rejection (Remarks p.19). The Examiner has maintained the rejection of claims that recite functional language as not enabled by the instant specification. While Applicant accuses the Examiner of trying to 'have it both ways' (Remarks p.19 ln.4), the Examiner asserts that in the interest of compact prosecution both the anticipatory and enablement rejections are set forth where it is unclear whether the recited functional limitations are an attempt to further limit that which is described by the specific structural limitations. Thus while the claims set forth structural limitations, in the instant case, in view of the assertions and specific teachings of the instant specification, the examiner maintains that the instant application is not enabled for a nucleic acid encoding an expression product that is broadly described as immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease, or multiple sclerosis.

Applicants have asserted (Remarks p.13-14), in response to the Examiners indication that the instant specification provides no analysis of the transcription/translation assay, that Applicants need not provide additional details of the technique. The Examiner maintains that it is unclear from the specification why a particular PCR product generated in the same manner using only different templates yields proteins with various molecular masses where the resulting PCR product is asserted to encode a specific polypeptide of a specific molecular mass. Given such a result it is unclear what polypeptide would in fact be 'recognized by antibodies from a patient suffering from an autoimmune disease'.

With regard to the analysis of a recombinant protein created from a nucleic acid comprising SEQ ID NO: 2 by exposure to sera from 'MS', 'Neurological Controls', and 'Healthy Controls', Applicants have remarked that 'the neurological controls are known, and the non-diseased control samples are known'. The Examiner maintains that it is not clear what is encompassed by a 'neurological control' (is this a subject without MS, a subject that has MS but no symptoms, a subject completely free of any neurological pathology) or a 'healthy control' (how is it determined that this person is healthy, are they specifically known not to have MS, can they be non-syptomatic MS patients and be considered healthy). With regard to the analysis of the sera reactivity, the Examiner maintains that Talbe 3 of the instant specification, where reactivity is simplified to indicate a plus (+) or minus (-) with regard to reactivity, merely indicates that more often that not the sera of an MS patient **does not immunologically recognize** the expression product from SEQ ID NO: 2. And while it is remembered that a US Patent

Application is not an FDA application to conduct clinical trials, without an analysis indicating that such reactivity occurs in a statistically relevant amount of either MS or any autoimmune patient, it is not apparent that one can characterize such an expression product as 'immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease'.

Applicants have requested clarification of the examiners comments regard the applicability of the claimed nucleic acid expression product to other species and whether the claims need to be limited to humans (remarks p.15 last¶). The Examiner maintains that the claims should be limited to humans. While the Applicant argues that the rejected claims are product claims derived from humans, the rejected claims require only an isolated nucleic acid molecule encoding an expression product where the expression product is characterized in that it is immunoligcally recognized by antibodies present in a biological sample from a patient (which encompasses ***any*** type of patient) suffering from an autoimmune disease. Thus the functional limitations of the claims are not limited to humans. For example, would the expression product of the claims be 'immunologically recognized' by antibodies from a chimpanzee (where page 16 of the Remarks appear to indicate that *P. troglodytes*do not have ORFs for gag protein) with MS or any other autoimmune disease. Is there any evidence that the claimed expression product would be recognized by antibodies from, for example, and aardvark, platypus, or koala bear?

Applicants have argued the application of the references of Newton et al, Chan et al, Lucentini, and Thisted. Initially it is noted that the currently amended claims do not

have the same functional limitations of the previously presented claims which required, for example, association of a gene or transcript with various pathological conditions. For the sake of clarity of the record it is noted that Newton is applied by the Examiner for its teachings indicating that results pertaining to sera reactivity can not be readily applied to the functionality of a transcript or the amount of a transcript in a pathological condition, where similar teachings are provided by the Chan reference. The references of Lucentini and Thisted are provided to indicate what is properly required to indicate that there is, for example, a reliable association between immunological recognition of an expression product and the presence of an autoimmune disease. Taking into account the teachings of Lucentini (where association studies require large sample sizes and family studies) and Thisted (where a p-value of less that 0.05 is required for significance), that data presented in Table 3 is not considered sufficient to characterized the expression product encoded by SEQ ID NO: 2 as immunoligaclly recognized by antibodies from a patient with an autoimmune disease of MS. In fact, as mentioned above, given the data from Table 3 alone, it is perhaps more appropriate to consider the expression product encoded by SEQ ID NO: 2 as a product that is ***not*** recognized by antibodies from an autoimmune patient.

Thus given the teachings of the specification and the requirements of the claim, the Examiner maintains that the specification is not enabling for a nucleic acid encoding an expression product that is immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease.

The rejection is MAINTAINED.

Claim Rejections - 35 USC § 102 – New Grounds of Rejection

The claims of the instant application are broadly drawn to nucleic acid fragments. In examination of the claims, the recitation of an intended use is not considered a significant limitation of the claim. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim (see MPEP 2112).

Additionally, it is noted that the claim limitations that characterize a nucleic acid fragment as 'encoding an expression product' are interpreted as broadly as they are written. All polynucleotides encode expression products in so far as all polynucleotides may be transcribed e.g. to create an RNA expression product), and all RNA expression products that comprise an amino acid encoding triplet codon may be translated (to create a polypeptide expression product).

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-3, 5, 6, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796) (1995).

3. This rejection is made based on the limitation of part (iii) of claim 1 which requires '***a*** sequence complementary to sequence (i) or (ii)' (emphasis added), where the limitation encompasses any sequence that has complementarity to any part of the structures required by parts (i) or (ii) of claim 1. The rejections may be overcome by changing the recited phrase to '***the*** sequence ***fully*** complementary to sequence (i) or (ii) (emphasis added).

Brennan teaches a microarray that contains 10-mer polynucleotides spotted at a discrete location such that the total array represents every possible permutation of 10-mer oligonucleotide (col. 9, lns. 48-55). Such an array would inherently comprise any 10-mer nucleic acid (see for example Fig 1b of Brennan which demonstrates the manner in which a 3-mer array comprises every possible 3-mer nucleic acid), including nucleic acids claimed in the instant application.

Regarding claim 1, the array of Brennan, due to its comprehensive nature, includes a 10-mer of the sequence GTAGTCGTAT. Such a sequence is a sequence complementary to nucleotides 1-10 of SEQ ID NO: 2, and thus satisfies the limitations of part (iii) of claim 1.

Regarding claims 2-3, the array of Brennan contains the nucleic acids of claim 1 which are inherently present in chromosome 3.

Regarding claims 5 and 6, the limitations of claims 5 and 6 serve to further limit the expression product that is recited in part (ii) of claim 1, which does not effect the manner in which the oligonucleotides of Brennan satisfy the limitations of part (iii) of claim 1.

Regarding claim 16 the nucleic acid array of Brennan comprises a nucleic acid which satisfies the required limitations of claim 1, and thus is a reagent comprising at least one isolated nucleic acid molecule according to claim 1.

Response to Remarks

Applicants have traversed the rejection of claims as anticipated by Brennan. Applicants have asserted that Brennan teaches only permutations of the particular oligonucleotide set forth as SEQ ID NO: 1 in Brennan. The Examiner maintains that the teachings of Brennan are drawn to creating an array in which every 10-mer oligonucleotide is represented, where the reference clearly indicates the comprehensive nature of such arrays in Fig 1b (which indicates how one may make a 3-mer array in which every 3-mer is represented). Thus Applicants assumption that Brennan teaches only permuations of SEQ ID NO: 1 (Remarks page 21) is not accurate, and the Examine maintains the interpretation of Brennan that the reference provides teaches from which one of skill in the art can envision an array of 10-mer oligonucleotides comprising every 10-mer oligonucleotide.

The rejection as set forth is MAINTAINED.

New Rejection

Claim Rejections - 35 USC § 102

4. Claims 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chanda et al (1981).

This rejection is made based on the limitations of the claim 7 which recite 'can be obtained by transcription of a nucleic acid molecule' where the claims encompass the transcription product generated transcription of any part of SEQ ID NO: 2. The

rejections may be overcome by amending the recited phrase to 'can be obtained by the complete transcription of an entire nucleic acid molecule'.

Regarding claims 7 and 21, Chanda et al teaches an RNA dinucleotide that is a transcription product and has the structure pppGpC (p.98, right col., Synthesis of pppGpC during transcription). A dinucleotide of such a structure could result from the transcription of nucleotides 17-18 of SEQ ID NO: 2, and thus satisfies the limitations of claim 7. Because Chanda et al teach a dinucleotide that satisfies the limitations of claim 7, the reference necessarily teaches a reagent comprising at least one transcription product according to claim 7, thus satisfying the limitations of claim 21.

Conclusion – Claim Objection

5. Claim 46 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claim 46 is drawn to an isolated nucleic acid comprising the sequence as set forth in SEQ ID NO: 2. The complete sequence set forth as SEQ ID NO: 2, which contains 2009 nucleotides, is not described in the prior art, and this 2009 bp sequence is not obvious in view of the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Kapushoc
Art Unit 1634

BJ FORMAN, PH.D.
PRIMARY EXAMINER